REMARKS

Claims 1-35 are pending in the application. Claims 8-10 and 17-35 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention. Claims 1-7 and 11-16 have been rejected. Applicant notes that the Examiner's notation throughout the Office action that claims 1-7, 11-17 are currently pending is a mistake and inconsistent with the previous restriction requirement.

Claims 1-35 have been cancelled and new claim 36 has been added. Support for the new claim 36 can be found throughout the specification and the claims as originally filed. Specifically, support can be found on page 3, lines 8-9 and on page 12, line 5. No new matter has been added by the proposed amendments. Cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the invention to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Objections

The Examiner objects to claims 1, 3-7, and16 because part of claims 1, 3-7, and 16 are drawn to a non-elected invention. This objection is moot in light of the cancellation of claims 1, 3-7, and 16.

The Examiner objects to claim 2 because it is not clear how the marker "corresponds" to a transcribed polynucleotide. This objection is moot in light of the cancellation of claim 2.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph.

Claims 15 is rejected under 35 U.S.C. § 112, second paragraph because it is drawn to "stringent conditions" which is not defined by the claim. This rejection is moot in light of the cancellation of claim 15.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-7 and 11-16 are rejected under 35 U.S.C § 112, first paragraph. Although these rejections are moot in light of the cancellation of claims 1-7 and 11-16, Applicants respectfully traverse this rejection to the extent that it may be applicable to the newly presented claim 36.

A. The Examiner asserts that "one cannot extrapolate the teaching in the specification to the enablement of the claims, because one would not know how to make the invention, due to the lack of disclosure in the claims and in the specification the actual sequence structure of ID-1 and ID-3." In response, Applicants have amended page 79 of the specification and submit herewith a revised sequence listing including the sequences of both ID-1 and ID-3 as SEQ ID NO: 4 and SEQ ID NO: 5, respectively.

The Examiner states that GenBank accession numbers could be updated and includes an interview summary with Eric Sayers, a GenBank representative. Applicant fails to see the relevance of this call to the GenBank representative as it is clear from examination of the GenBank Accession numbers that the two sequences at issue had not been modified prior to the mailing date of this office action (see attached printouts from GenBank). According to the GenBank website (http://www.ncbi.nlm.nih.gov/Sitemap/samplerecord.html.), while sequences can be updated, all modifications can be easily detected when the accession number is viewed. For example, the date in the LOCUS field is the **date of last modification** and any updates to the sequence (even a single base) increases the version number. Upon inspection of the two sequences in this application, X77956 and X69111, it can be easily seen that neither sequence has been modified since submission on January 19, 1995 and August 13, 1997, respectively.

Nevertheless, Applicants also submit herewith a Statement from the Applicants' representative stating that the amendatory material in the sequence listing consists of the same material incorporated by reference in the application as originally filed, as required by the Examiner.

B. The Examiner further states that "one cannot extrapolate the teaching in the specification to the enablement of the claims, because in the absence of objective evidence, one cannot predict that ID-1 and ID-3 polynucleotides have a decreased mRNA expression level in prostate cancer tissue as compared to normal prostate tissue." Applicants respectfully traverse this rejection.

The present invention is enabled since the experiments described in the specification were performed in a well-recognized *in vitro* model of human prostate cancer which is recognized by those skilled in the art to correlate with *in vivo* human results. The LNCaP cell line, which was established from a metastatic lesion of human prostatic adenocarcinoma, has been widely used in the study of prostate cancer for over 20 years. The enclosed seminal journal article establishes the LNCaP cell line maintains malignant properties, hormonal responsiveness and drug sensitivity of the prostate adenocarcinoma (Horoszewicz, J.S. "LNCaP Model of Human Prostatic Carcinoma" *Cancer Research*, 43, 1809-1818 (1983)). Those skilled in the art view LNCaP cells as an established *in vitro* model of prostate cancer as evidenced by the fact that this seminal article establishing the LNCaP cell line has been cited over 800 times in other peer-reviewed journals.

According to MPEP 2164.02, "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating." (See also, *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995), reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications).

In addition, Applicants submit concurrently herewith a Declaration of Dr. Steven Haney pursuant to 37 C.F.R. §1.132 to overcome these rejections. This Declaration establishes that one skilled in the art would recognize that the LNCaP cell line model used in the experiments described in the application is a well-characterized model of human prostate cancer and therefore, one can predict that since ID-1 and ID-3 expression was decreased in the LNCaP cell line model, expression would also be decreased in cancer tissue. Well-characterized human cancer cell lines, such as LNCaP, are routinely used and have proven to be highly predictive of *in vivo* results.

Furthermore, Applicants' specification is disclosed in such manner that one skilled in the art will be able to practice it without undue experimentation. The identified markers, ID-1 and ID-3, were found to be significantly ($p<0.05$) and differentially expressed between the diseased and normal tissues (See specification, page 8, line 20-22). In addition, the LNCaP well-established cell line model of human prostate cancer, was used to show that ID-1 and ID-3 decrease in expression in prostate cancer cells after androgen treatment. The prostate specific antigen (PSA) gene, which is recognized in the art as a diagnostic marker of prostate cancer, was used as an internal control showing that decreased expression of ID-1 and ID-3 corresponds to the expected increase in PSA expression in prostate cancer cells. Therefore, one skilled in the art would appreciate the accuracy with which the cell line model of prostate cancer mimics the genetics of human prostate cancer and further recognize the application's analytical techniques (e.g., RNA extraction, quantitative RT-PCR, western blot analysis, statistical analysis, and tissue microarray analysis) to be well established. One skilled in the art would conclude that the *in vitro* data presented by the applicant is well correlated with the invention as claimed, namely the methods of the invention to diagnose or monitor development or progression of prostate cancer in humans.

The Declaration and above remarks obviate the rejection under 35 U.S.C. § 112, first paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

C. The Examiner states that claims 1-7 and 11-16 are rejected for the use of the language "difference in the level of expression" in claim 1, or "the level of expression is significantly altered" in claim 16. This rejection is moot in light of the cancellation of claims 1-7 and 11-16.

D. The Examiner states that claims 1-7 and 11-16 are rejected for the use of the language "a portion" of ID-1 and ID-3 polynucleotides. This rejection is moot in light of the cancellation of claims 1-7 and 11-16.

E. The Examiner states that claims 1-3, 6-7, 11-16 are rejected for not restricting the sample to include a specific cell type. Although the rejection is moot in light of the cancellation of the claims, Applicants point out that the new claim 36 recites "in a sample of prostate cells."

CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. In the event that the amendments and remarks are not deemed to overcome the grounds for rejection, the Examiner is kindly requested to telephone the undersigned representative to discuss any remaining issues.

Respectfully submitted,

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